ICP

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/874,475	06/04/2001	Christos J. Petropoulos	2793/65166/JPW/JML/CMR	5338

7590 06/01/2004

Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
WINKLER, ULRIKE	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,475	PETROPOULOS ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-71 and 73-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-71 and 73-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/30/03 & 4/13/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The request filed on April 13, 2004 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/874475 is acceptable and a RCE has been established. Claims 38-71, 73-88 are pending and are currently under prosecution. An action on the RCE follows.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed December 30, 2003 and April 13, 2003 are attached to the instant Office Action.

Claim Rejections - 35 USC § 112

The rejection of claims 38-71 and 73-88 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is withdrawn** in view of Applicant's amendment to the claims canceling the limitation "patient derived viral envelope protein and nucleic acid".

The rejection of claims 38-71 and 73-88 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is withdrawn** in view of Applicant's amendment to the claims canceling the limitation "patient derived viral envelope protein and nucleic acid".

The rejection of claim 72 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of Applicant's cancellation of the claims.

Claim Rejections - 35 USC § 102

The rejection of claim 72 under 35 U.S.C. 102(b) as being anticipated by Petropoulos et al. (Antimicrobial Argents and Chemotherapy, April, 2000) **is withdrawn** in view of Applicant's cancellation of the claims.

New rejections in view of Applicant's amendments to the claims:

Claim Rejections - 35 USC § 112

Claims 38-71 and 73-88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The dictionary definition of the term "plurality" is: a state of being numerous or a state of being plural or a large number or quantity. The term "plural": constituting a class of grammatical forms used to denote more than one or in some languages more than two or containing more than one or more than one kind of class [see Webster's dictionary 10th edition]. Therefore based on the definition from the dictionary "a plurality" can simply be two of the same kind or it could be interpreted to be two of different kinds. As there is no definition for the term "plurality" in the specification. For purposes of the instant Office action the term "plurality" is interpreted as being more than one different kind for the purpose of

the enablement rejection below and the term is "plurality" is interpreted as being more than one same kind for the purpose of the reinstated art rejection below.

Claims 38-71 and 73-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The newly amended claims are rejected because of the new limitation "plurality" "plurality of cells" "plurality of viral particles" and "plurality of envelope proteins" are not supported in the specification, there is no literal support for the term "plurality" in the specification as filed.

Claim Rejections - 35 USC § 103

Claims 38-71 and 73-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al. (Journal of Virology, 1996), Petropoulos et al. (Antimicrobial Agents and Chemotherapy, April 2000) in view of Grovit-Ferbas et al. (Journal of Virology, 1998) and Trkola et al. (Journal of Virology, 1999). The prior withdrawn rejection is now reinstated in view of Applicant's amendment to the claims.

Applicant's response addressed how the amended claims would not apply to the instant rejection. Applicants are interpreting the term "plurality" to indicate multiples of different kinds, while the Office is interpreting the term to be merely just multiples of the same kind (see 35 U.S.C. 112, second paragraph rejection above).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants addressed each references and indicated that none of the references teach multiple envelope constructs.

Gao et al. teaches the use of single round virus infectivity assay utilizing patient derived amplified env segments. ln this assay the patient derived env gene pSVIII-gp160 constructs which expressed functional envelope under the control of H1V-1 long terminal repeat promoter. pSV111-gp160 were co-transfected with HXBHIOAenV CAT into Cos-cells. HxBllloAenv CAT is an *env* deficient provirus, which contains a chloramphenicol acetyltransferase (CAT) gene in place of the *env* gene. After culturing in the Cos cells the produced virions are collected and used to infect new' donor derived peripheral blood mononuclear cells (PBMC), the cells were then assayed for the presence of CAT activity (see page 1654, material and methods). The proposed utility for the generated envelope clones includes the use of the constructs for the analysis of fusion enhancement *env* complementation and infectivity assays (see page 1665, last paragraph). The assay disclosed in the reference utilizes obtaining a nucleic acid sequence into pSVII1-gp160. Co-transfecting a cell (Cos cells) with a viral expression vector and the viral envelop sequence, collecting the particles produced from the cell and contacting the viral particle with PBMC, measuring the amount of signal produced (CAT). Though the reference suggest the use of these envelope constructs for studying infectivity the reference did not disclose a step-by-step assay to assay a compound for the ability to inhibit viral entry into a permissive cell.

Petropoulos et al. teach a single cycle transfection assay with HIV vectors in which a

patient sample can be tested for the sensitivity to a compound. In this assay the patient derived sample involves the HIV polymerase gene. The reference discloses a resistance test vector that contains *gag/pol* but has the envelope region deleted and the luciferase reporter gene inserted instead, this is referred to as the resistance test vector. The reference uses an amphotropic MLV *env* DNA segment that is on a second vector, which will produce particles that have a reduced risk of recombination event for producing fully infectious HIV particles (see page 922, figure 1). This assay set up reduces the risk to laboratory personal. The reference teaches an assay that tests for the effectiveness of compounds and their ability to inhibit HIV replication. The assay allows for monitoring the frequency of drug resistance virus transformation in a patient sample. The assay can be used to screen for new dnzgs that are active against HIV resistant strains (see page 926, last paragraph). The reference does not teach analyzing patient derived HW env segment for their ability to infect new cells and for compounds that may inhibit the viral entry.

Grovit-Ferbas et al. teach the production of chimeric full-length viruses in which patient derived *env* segments are inserted into the virus. These viruses are than assayed for their co-receptor usage (see material and methods) the osteosarcoma cells expressing CD4 and one of the following chemokine receptors; CCRI, CCRZ, CCR3, CCR4, CCr5, GPR15 (BONZO), STRL33 (BOB) or CXCR4. The reference teaches a cell line that can be modified with various co-receptors and that each patient sample must be assayed for the ability to utilize the various correctors for entry. The differences in replication kinetic is linked to the efficiency of viral entry The premise of the study is that genetic differences in viral envelope sequences which result in inefficient entry into cells may be important determinants in long-term survival. The study specifically looks at identifying viral isolates with their respective coreceptor usage. The

reference does not teach assaying compounds for their ability to interfere with viral entry.

Trkola et al. teach the use of antibodies as a compound for inhibiting the entry of a viral particle into a host cell. The reference teaches the use of neutralization assay for the analysis of primary H1V-I isolates. The reference does not teach analyzing amplified *env* segments from patient derived samples for their ability to be inhibited by antibodies.

It would have been obvious to one of ordinary skill in the art 4t the time the invention was made to test a patient derived HIV sample for the ability to be inhibited by a compound that will prevent viral entry. One having ordinary skill in the art would have been motivated to do this in order to develop a drug regime that is specific for the patient. By determining if the patient derived virus has mutated in such a way as to be resistant to the drug regime that the patient is being treated with, it would have been obvious to one having ordinary skill in the art to monitor antiretroviral therapies. This information is clinically valuable by providing reliable assessment of the viral burden and is useful in monitory the clinical efficacy of the treatment. Gao et al. teach a single round infectivity assay that utilizes various patient derived and amplified env segments, the reference utilizes CAT as the indicator gene which is found on the resistance test vector which also comprises the g*ag/pol* gene sequences but has the *env* sequence deleted. The reference teaches that different *env* sequences have different biological characteristics. The env clones can be utilized in envelope complementation and infectivity assays. Petropoulos et al. teach an assay for testing drug susceptibility, the assay utilizes a resistance test vector comprising g*ag/pol* sequences and a *env* vector for the production of viral particles from cotransfected cells. Grovit-Ferbas et al. teach that different viral envelope sequences have different effects on the ability of a viral particle to enter a host cell. Those viruses that have

diminished capacity to enter a new host cell are found in long term HIV survivors, indicating that reducing the ability of a new particle to enter the next host cell will be beneficial for increasing the survival of an HIV infected person. The reference also teaches assaying each viral envelope sequence for the usage of different coreceptors. While the Trkola et al. reference teaches an assay that determines if an antibody is able to inhibit the entry of a viral particle into a new host cell. The prior art teaches assays that focus on the HIV viral envelope protein and indicate preventing viral entry by blocking the association of the viral envelope with the cell surface receptor is desirable drug target. It is well established in the prior art that HIV has a high mutation rate, especially in the envelope region, hence vaccines have not been successful due to the changing envelope structure of the virus. The prior art also indicated that for any therapy to be effective it is necessary to assay the changes in the virus population in a patient and follow the mutations that occurs when applying drug therapy. This will ensure that the patient is treated with the best possible drug combination that is effective for the virus the patient harbors at any point. Therefore, the instant invention is obvious over Gao et al. and Petropoulos et al. in view of Grovit-Ferbas et al. and Trkola et al.

Conclusion

No claims allowed.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PHD.
PATENT EXAMINER
5/28/04